Uncomplicated urinary tract infection in women

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Uncomplicated Urinary Tract Infection

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How this article was created

We searched Medline and the Cochrane Library to identify published systematic reviews and randomised controlled trials on the diagnosis and management of uncomplicated urinary tract infections, including antibiotic benefits and harms, natural history of the condition, and commonly used alternative treatments (cranberry, urinary alkalisers, non-steroidal anti-inflammatory drugs). We included journal articles identified in the references of articles from the initial search. We searched for relevant NICE guidelines on uncomplicated urinary tract infections. We have referred to recent systematic reviews and meta-analyses but have cited individual clinical studies where there is no higher quality of evidence.

Contributorship and the guarantor

TH and CDM conceived the article and are guarantors. All authors wrote and reviewed the article and created the boxes.

How patients were involved in the creation of this article

We discussed the article with 2 women who have had uncomplicated urinary tract infections and ensured that information was provided about whether alternatives to antibiotics work and that contained Box 5 safety-netting information and prompted that written information be provided.

Conflicts of Interest

TH and CDM have received funding from the Australian National Health and Medical Research Council for research on reducing antibiotic resistance for acute infections and for shared decision making, and from the Australian Commission on Safety and Quality in Health Care for the development of shared decision making resources. MB has no competing interests to declare.

Licence

Uncomplicated Urinary Tract Infection

Vignette/case and introduction

Your next patient is a 32 year old woman who thinks she has a urinary tract infection (UTI). She's passing urine more frequently, has suprapubic pain and dysuria. After two days, it hasn't improved.

This article will outline how to identify uncomplicated UTI in adult non-pregnant women (18-65 years) and discuss options with women to help them make an informed decision about its management.

What you should cover

Acute UTIs are very common community infections. They affect most women at least once in their life and far less prevalent among men.[1-3] Women with an acute UTI present with diverse symptoms that can be burdensome and impact their quality of life.[4 5]

What questions you should ask

Take a history to determine risk factors for UTI and differentiate between uncomplicated UTIs and other causes of urinary symptoms. Recurrent UTI (when there are 3 or more UTIs within one year), asymptomatic bacteruria, or infection associated with an indwelling urinary catheter each require a different approach, not covered here. Symptoms and signs are described in box 1. Evidence from diagnostic studies supports the useful diagnostic value of commonly recognised symptoms such as dysuria, haematuria, nocturia, urgency and frequency, as well as those that decrease the probability that the patient has a UTI. Likelihood ratios of these symptoms are listed in box 2. However, no individual or combination of symptoms can make clinicians completely confident in diagnosing a UTI. Check for red flags suggestive of acute pyelonephritis or sepsis (box 3), which would require immediate management and/or referral to a hospital.

Is examination necessary?

In most cases of low-risk non-pregnant women with UTIs, clinical examination is not required, and the consultation can be safely conducted remotely. However, if the patient is systemically unwell and presents with any red flag symptom, arrange a physical examination. Assess the patient's vital signs (temperature, blood pressure, heart rate, and respiratory rate) for signs of systemic illness or sepsis and palpate the abdomen and the back for flank or suprapubic tenderness.

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Box 1. Questions to ask

Is the patient experiencing:

- Burning pain while urinating (dysuria)?
- Urge to void immediately (urgency)?
- Passing urine more than usual at night (nocturia)? Or passing urine more frequently in general (frequency)?
- Cloudy urine visible to the naked eye or blood in the urine (haematuria)?

Vaginal discharge and/or vaginal irritation? (these symptoms are suggestive of a vaginal cause of urinary symptoms. Box 4 gives the most common differential diagnoses for UTIs.)

NICE Guidelines state that patients with 2 or 3 of these key symptoms (cloudy urine, dysuria or new nocturia) are indicative of a UTI.[9 10] However a systematic review of 16 studies (3711 patients)[11] identified visible haematuria (rather than cloudy urine), along with dysuria or new nocturia, as one of the diagnostic symptoms suggestive of UTI.

Is there a history of:

- recent sexual activity? (UTIs are very common among sexually active women.[6])
- previous UTI? (The majority of women with a UTI reported a history of UTI infection during the 12 months prior to the current episode.[7])
- Using spermicidal agents or a diaphragm? (Spermicidal agents affect the vaginal flora and the diaphragm increase the levels of introital and periurethral colonization with bacteria.[8])
- Current pregnancy? (UTIs are common during pregnancy)
- Diabetes? (UTIs are more frequent in patients with type 2 diabetes.[6])

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Box 2: Summary likelihood ratios (LR) of symptoms suggestive of an uncomplicated UTI[11, 12]

Symptoms INCREASING the probability of UTI *	Symptoms DECREASING the probability of UTI **
• Haematuria +LR 1.72 (95% CI 1.30 to 2.27)	• A history of vaginal discharge +LR 0.3 (95% CI 0.1 to 0.9)

• Dysuria +LR 1.30 (95% CI 1.20 to 1.41) • Nocturia +LR 1.30 (95% CI 1.08 to 1.56) • Urgency +LR 1.22 (95% CI 1.11 to 1.34) • Frequency +LR 1.10 (95% CI 1.04 to 1.16)	• A history of vaginal irritation +LR 0.2 (95% CI 0.1 to 0.9)
* All values reported for threshold of $\geq 10^2$ CFU/ml, therefore probabilities at higher reference standards are lower. ** Values reported for threshold of $\geq 10^5$ CFU/ml	

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Box 3: Red flags for acute pyelonephritis or sepsis	
Acute pyelonephritis[6 13]	**Sepsis**[14]
• Flank pain (on the back, at and/or below level of ribcage) • Rigors or fever >37.9°C • Nausea/vomiting • New/different myalgia, flu-like illness	• ≥ 21 breaths per minute • Heart rate: ≥ 91 beats per minute • Systolic blood pressure 91-100 mmHg or less than 90 mmHg (i.e. > 40 mmHg below normal) • Not passed urine in the past 12-18 hours or more • Behaviour changes (acute deterioration, altered behaviour or mental state)

Box 4: Common differential diagnoses of urinary symptoms[12]
• Vaginal infections (e.g., Trichomonas, Candida albicans, Gardnerella) • Vaginitis: post sexual intercourse, irritants • Sexually transmitted infections leading to pelvic inflammatory disease • Vulvovaginal atrophy

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106 **What investigations might be needed?**

107 Urine dipstick tests are the most commonly used point of care test in primary care.[15] For the
108 laboratory diagnosis of UTI, dipstick results can modestly improve diagnostic precision, but
109 cannot definitively rule out a UTI (Table 1).

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Table 1. Investigations for uncomplicated UTI in 18-65 year old non-pregnant women[15]					
Number of these symptoms present (Dysuria, new nocturia and cloudy urine / haematuria present)	**Dipstick urinalysis**			**Possibility of UTI**	**Further testing**
	Nitrite	Leukocyte	RBC		
2 or 3	May not be needed[10]			Highly likely	urine culture typically not needed
1	+	-	+	Likely* [15]	Send urine for culture[t]
	+	+	-		
	+	-	-	Likely**	
	-	+	+		
	-	+	-	Equally likely to other diagnosis	
	-	-	-	Less likely***	No indication for urine culture
*Positive predictive value (PPV) of 92% (95% CI 86 to 96%), which is the probability that patients with a positive test have a UTI. Cut-off point on dipstick score ≥3 (NPV= 42%, 95% CI not reported). ** Positive predictive value of 81% (95% CI= 77% to 84%). Cut-off point on dipstick score ≥ 2 (NPV =57%, 95% CI 52 to 62%) *** Negative predictive value (NPV) 76% (95% CI 66 to 84%) which is the probability that patients with a negative test truly do not have a UTI. Cut-off point on dipstick score ≥1 **Urine dipstick cut-off score** is based on the sum of nitrite = 2, leucocyte = 1.5, RBC = 1.					

[t] Growth cut-off thresholds used to define a UTI can vary (e.g. in some laboratories or countries, it may be ≥10^3 CFU/ml, whereas ≥10^5 CFU/ml in others). Culture results should also be interpreted with consideration of the severity of signs and symptoms.	

What you should do

Constructing a shared decision making conversation

In this scenario there are typically two main options that are reasonable to consider: immediate antibiotics or 'wait and see'/delayed prescribing. To enable the patient to make an informed decision about the next steps, the clinician needs to explain both options to the patient, along with the benefits and harms of each, and discuss the patient's preferences before making a shared decision. An approach to this is suggested in box 5.

What is the natural history of a UTI?

There is uncertainty around the natural history of uncomplicated UTI, with few studies examining this. In a systematic review of the placebo-controlled arms of three randomised trials (346 placebo group participants), some women appeared to improve or become symptom free spontaneously, with most improvement occurring in the first 9 days.[16] Over the first 9 days, the percentage of participants who were symptom free or reported improved symptoms was reported as rising to 42% and by 6 weeks, the percentage was 36%. Some women (39%) whose symptoms either failed to improve by 6 weeks or became worse over a variable timespan, although the rate of serious complications was low with progression to pyelonephritis was reported in one placebo participant in two of the trials. The low rate of serious complications supports the practice of delayed prescribing, where the patient is given a prescription but advised to wait to see whether symptoms self-resolve before antibiotics are commenced.

An estimate of the mean duration of UTI symptoms is provided by an observational study of women with suspected uncomplicated UTI.[18] In the 511 women who had seen a clinician for their symptoms and rated the initial problem as moderately bad or worse, the mean reported symptom duration was 3.8 days. However, most of the sample took antibiotics, with only 17 participants (approximately 3%) who did not; their reported mean symptom duration was 4.9 days. In a related 5-arm randomised trial, a similar duration of moderately bad or worse symptoms was reported: 3.5 days in the immediate antibiotic group and 4.8 days in the delayed (by 48 hours) prescription group.[19]

How long can you 'wait and see' for?

The recommendation in the NICE guideline[17] is to wait for 2 days before commencing antibiotics. However, there is no evidence provided in support of this timeframe and it is unclear whether the 2-day timeframe is from the start of symptoms or from first consultation. The findings from the systematic review[16] suggest a 2-day timeframe may be too short, with few participants likely to have improved by then, although about a third may have improved by 7–10 days. There appears to be a lot of uncertainty and variability in the spontaneous recovery timeframe, and when 'wait and see' (delayed prescribing) is discussed with the patient as an option this should include careful description of when to reconsult or commence antibiotics (Box 5).

The option of a delayed prescription will be acceptable to many patients. In a cohort study in Amsterdam, 37% of women who were asked by their general practitioner to delay antibiotic treatment were willing to do so,[20] however no further details about how this option was presented to patients are provided.

What difference do antibiotics make?

Surprisingly, we could not find a synthesis of antibiotic versus placebo randomised controlled trials for uncomplicated UTI in women under 65 years and therefore no quantification of the effect, perhaps because antibiotic treatment is the traditional management of uncomplicated UTI. The extent to which they reduce recovery time, reduce the risk of progression to pyelonephritis, and reduce the risk of recurrence is unknown and not presented in evidence-based clinical practice guidelines.

For the antibiotics most commonly prescribed for UTI (e.g. nitrofurantoin, trimethoprim), there does not appear to be synthesised evidence of their harms. For other antibiotics commonly prescribed in primary care, commonly reported adverse effects include diarrhoea, rash, and nausea.[21 22] Candidiasis is also possible from antibiotic use. Another harm of antibiotic use is the contribution to antibiotic resistance. This is already particularly a problem for trimethoprim, with existing resistance rates of at least 30% of *Escherichia coli* isolates to trimethoprim.[23] Patients with antibiotic-resistant *E. coli* UTI are significantly more like to experience clinical response failure (odds ratio [OR] 4.19 (95% confidence interval 3.27 to 5.37); n = 2432 participants).[24]

Despite being unable to quantify how much difference antibiotics make to UTI symptom duration, they are effective in treating the infection. Refer to the current NICE guideline for information about considerations about which antibiotic (guided by local antibiotic resistance patterns, where possible), and recommended dosage and duration.[17]

Other treatments

There is little evidence to support the various over-the-counter medications that patients will often have tried prior to a consultation or concurrently with antibiotics. A 2016 Cochrane review of urinary alkalisers found no randomised trials.[25] There are no randomised trials of cranberry for the treatment of uncomplicated UTI[26 27] and a Cochrane review of cranberry products found they did not prevent recurrent urinary tract infections in women any more than placebo or no treatment (RR 0.86, 95% CI 0.71 to 1.04).[28]

A systematic review of the effectiveness of non-steroidal anti-inflammatory drugs (NSAIDs) compared to antibiotics for uncomplicated UTI found five randomised trials.[29] For the outcome of symptom resolution, three trials found that NSAIDs were inferior to antibiotics; but two trials (smaller, with higher or unclear risk of bias) found no significant difference between the arms. In the groups that received NSAIDs, the percentage of women with symptom resolution by day 3 or 4 ranged from 39%-58%. In two of the three trials that reported pyelonephritis, rates were slightly higher in the NSAID group (risk difference of 4 and 5 respectively).

When to reconsult and when to refer

Women with uncomplicated UTI without risk factors can be typically be assessed remotely. Box 5 contains safety-netting information to advise patients about when to commence antibiotics (if a delayed prescription was given) and/or reconsult and Box 3 lists the red flags for acute pyelonephritis and sepsis which are likely to require hospital admission.

Box 5: Elements of a shared decision making conversation

A shared decision making discussion following the diagnosis of an uncomplicated UTI typically involves the following (although it may not be a simple linear process as presented here):

- **Outline that there is choice about the next steps** and a decision to be made; **invite** the patient to partner with you in the decision-making to the extent that the patient desires, and reassure any patient who feels overwhelmed or uncertain about the patient's involvement or how to proceed;
- **Elicit the patient's expectations about management of the condition**. This can include previously tried treatments and experiences, along with fears and concerns (including symptom severity and how it may impact daily tasks); this allows for

detecting and discussing misperceptions, where necessary, either now or later in the process);

- **Explain the options**
  - Wait and see (this may involve providing a delayed prescription for antibiotics and clear information about to when to use it)
  - Commence antibiotics immediately
- **Discuss the benefits and harms of the options** (including their likely probability or size)
  - Describe the natural course of an uncomplicated UTI and that for some women, it will resolve within about a week without taking antibiotics. Also explain that there is uncertainty about exact timeframes and whether your patient will be one of the women who gets better without antibiotics (and that if not, antibiotics may need to be commenced later).
  - Discuss that antibiotics probably shorten the duration of symptoms, however by taking them, there is the risk of side effects and antibiotic resistance.
  - Regardless of which option is chosen, provide advice on symptom management (e.g. paracetamol or ibuprofen)
- Provide the opportunity to **weigh up the benefits and harms of the options**, and consider them in the context of the patient's **preferences, values, and circumstances**
- **Explore if the patient has any questions**, is ready to make a decision, or needs further information, time, or the involvement of other people.
- Provide **safety-netting information** about when to commence antibiotics (if delayed prescription) and/or reconsult
  - Nausea or vomiting
  - Rigors
  - Shivering, chills, and muscle pain
  - Feeling confused or very drowsy
  - Not passing urine all day
  - Blood in the urine
  - Temperature above 38ºC
  - Kidney pain in the back or under the ribs
  - Worsening UTI symptoms
  - If taking antibiotics, no improvement in UTI symptoms after 48 hours
- Provide written **patient information leaflet** with summary information[30]

What you need to know

- In about a third of women, an uncomplicated UTI may resolve on its own within about 7-10 days, without the need for antibiotics
- The option of 'wait and see' (which typically involves providing a delayed prescription) can be discussed as part of a shared decision making process within the consultation
- Consider pyelonephritis or sepsis and hospital admission in patients who are systemically unwell and have high fever, rigours, nausea/vomiting, flank pain, low blood pressure, high heart rate, high respiratory rate, not passing urine for 12-18 hours, and behaviour change

Education into practice

How do you invite patients to share in the decision-making about management of their uncomplicated UTI, including a discussion about their expectations?

How can you facilitate a balanced discussion about the benefits and harms of using antibiotics immediately or adopting a 'wait and see' (delayed prescribing) approach?

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